AMENDMENTS TO THE CLAIMS:

Please amend claims 28 and 29 and add claims 90 - 94 as follows. This listing of claims replaces all prior listings of claims.

LISTING OF CLAIMS:

1. (Previously Presented) A fusion protein, comprising a nucleotide binding domain (DBD) operatively linked to a modified ligand binding domain (LBD) from an intracellular receptor, wherein:

the fusion protein is a ligand activated transcriptional regulator;

the nucleotide binding domain is a polydactyl zinc-finger that contains at least three modular portions thereof;

each modular portion of the nucleotide binding domain interacts with a contiguous sequence of nucleotides of at least about 3 nucleotides; and

the ligand specificity of the LBD for endogenous and exogenous ligands is modified to change its ligand specificity compared to the ligand specificity of the ligand binding domain of the native hormone receptor, whereby ligands that activate the fusion protein are not the ligands that activate the receptor from which the LBD was derived .

2. (Original) The fusion protein of claim 1, further comprising an operatively linked transcription regulating domain.

3. (Original) The fusion protein of claim 1, wherein the intracellular receptor is a nuclear hormone receptor.

4. (Cancelled)

5. (Previously Presented) The fusion protein of claim 1, wherein the modified ligand-binding domain is not substantially activated by endogenous ligands relative to exogenous or non-natural ligands.

6. (Previously Presented) The fusion protein of claim 1, wherein a module of the zinc-finger peptide binds to a sequence of nucleotides of the formula $(GNN)_n$, where G is guanidine, N is any nucleotide and n is an integer from 3 to 6.

7. (Cancelled)

8. (Previously Presented) A fusion protein of claim 1, wherein:

the nucleotide binding domain comprises at least 6 modular portions of a polydactyl zinc-finger peptide, wherein each modular portion thereof interacts with a contiguous

nucleotide sequence of at least about 3 nucleotides, whereby the nucleotide binding domain has unique specificity for a targeted gene;

the zinc-finger peptide is comprised of modular units from a C2H2 zinc-finger; and

the fusion protein is a gene-specific ligand activated transcriptional regulator.

9. (Cancelled)

10. (Previously Presented) The fusion protein of claim 1, that comprises at least four zinc fingers or variants thereof.

11. (Original) The fusion protein of claim 1, wherein the intracellular receptor is a nuclear hormone receptor selected from the group consisting of estrogen receptors, progesterone receptors, glucocorticoid-α receptors, glucocorticoid-β receptors, mineralocorticoid receptors, androgen receptors, thyroid hormone receptors, retinoic acid receptors, retinoid X receptors, Vitamin D receptors, COUP-TF receptors, ecdysone receptors, Nurr-1 receptors and orphan receptors.

12. (Original) The fusion protein of claim 1, wherein the intracellular receptor is a steroid receptor.

13. (Previously Presented) The fusion protein of claim 3, wherein the hormone receptor is a progesterone receptor variant or an estrogen receptor variant.

14. (Original) The fusion protein of claim 2, wherein the transcription regulating domain comprises a transcription activation domain.

15. (Original) The fusion protein of claim 2, wherein the transcription regulating domain comprises a transcription activation domain selected from the group consisting of VP16, VP64, TA2, STAT-6, p65 and derivatives, multimers and combinations thereof that have transcription activation activity.

16. (Original) The fusion protein of claim 14, wherein the transcription regulating domain comprises a nuclear hormone receptor transcription activation domain or variant thereof that has transcription activation activity.

17. (Original) The fusion protein of claim 14, wherein the transcription regulating domain comprises a steroid hormone receptor transcription activation domain or variant thereof.

18. (Previously Presented) The fusion protein of claim 14, wherein the transcription regulating domain comprises a viral transcription activation domain or variant thereof that has transcription activation activity.

19. (Original) The fusion protein of claim 18, wherein the transcription regulating domain comprises a VP16 transcription activation domain or variant thereof.

20. (Previously Presented) A fusion protein of claim 1, further comprising a transcription regulating domain that comprises a transcription repression domain.

21. (Original) The fusion protein of claim 20, wherein the transcription repression domain is selected from the group consisting of ERD, KRAB, SID, Deacetylase, and derivatives, multimers and combinations thereof such as KRAB-ERD, SID-ERD, $(KRAB)_2$, $(KRAB)_3$, KRAB-A, $(KRAB\text{-}A)_2$, $(SID)_2$ (KRAB-A)-SID and SID-(KRAB-A).

22. (Previously Presented) A fusion protein comprising a sequence of amino acids encoded by the sequence of nucleotides set forth in any of SEQ ID Nos. 1-18.

23. (Original) A nucleic acid molecule, comprising a sequence of nucleotides encoding the fusion protein of claim 1.

24. (Original) A nucleic acid molecule, comprising a sequence of nucleotides encoding the fusion protein of claim 2.

25. (Previously Presented) A nucleic acid molecule encoding a fusion protein of claim 1, wherein:

the fusion protein comprises a C7 C2H2 nucleotide binding domain operatively linked to a ligand binding domain from an estrogen receptor, which are encoded by a sequence of nucleotides set forth in SEQ ID No. 1.

26. (Original) A vector, comprising a sequence of nucleotides encoding the fusion protein of claim 1.

27. (Original) A vector, comprising a sequence of nucleotides encoding the fusion protein of claim 2.

28. (Currently Amended) ~~A~~ An isolated cell, comprising the expression vector of claim 26.

29. (Currently Amended) ~~A~~ An isolated cell, comprising the expression vector of claim 27.

30. (Original) The cell of claim 28 that is a eukaryotic cell.

31. (Original) The cell of claim 29 that is a eukaryotic cell.

32. (Previously Presented) A viral vector comprising a sequence of nucleotides encoding a fusion protein, wherein:

the fusion protein comprises a nucleotide binding domain operatively linked to a ligand binding domain from an intracellular receptor, wherein the nucleotide binding domain is a polydactyl C2H2 zinc-finger peptide or modular portion thereof that interacts with a contiguous nucleotide sequence of at least about 9 nucleotides; and

the fusion protein is a ligand activated transcriptional regulator.

33. (Original) The vector of claim 27 that is a viral vector.

34. (Previously Presented) The vector of claim 32, wherein the viral vector is derived from a DNA virus or a retrovirus.

35. (Original) The vector of claim 34 that is selected from the group consisting of an adenoviral vector, and adeno-associated viral vector, a herpes virus vector, a vaccinia virus vector and a lentiviral vector.

36. (Cancelled)

37. (Previously Presented) The vector of claim 33, wherein the viral vector is derived from a DNA virus or a retrovirus.

38. (Original) The vector of claim 37 that is selected from the group consisting of an adenoviral vector, and adeno-associated viral vector, a herpes virus vector, a vaccinia virus vector and a lentiviral vector.

39. (Previously Presented) A combination, comprising:

a fusion protein of claim 1; or

a nucleic acid molecule comprising a sequence of nucleotides that encodes the fusion protein; and

a regulatable expression cassette that comprises at least one response element recognized by the nucleic acid binding domain of the fusion protein.

40. (Cancelled)

41. (Original) The combination of claim 39 that comprises a single composition that contains the fusion protein or nucleic acid molecule that encodes the fusion protein, and the regulatable expression cassette in a pharmaceutically acceptable excipient.

42. (Original) The combination of claim 39, wherein the fusion protein or nucleic acid molecule comprising a sequence of nucleotides that encodes the fusion protein, and the regulatable expression cassette are in separate compositions.

43. (Cancelled)

44. (Previously Presented) The combination of claim 41, wherein the composition is formulated for single dosage administration.

45. (Cancelled)

46. (Original) The combination of claim 39, wherein the regulatable expression cassette comprises 3 to 6 response elements.

Claims 47-68 (Cancelled)

69. (Previously Presented) The fusion protein of claim 1, wherein the nucleic acid binding domain interacts with a contiguous sequence of nucleotides of about 18 nucleotides.

70. (Original) A non-viral delivery system, comprising the fusion protein of claim 1 or a nucleic acid molecule encoding the fusion protein.

71. (Original) The non-viral delivery system of claim 70, further comprising a nucleic acid molecule that comprises an expression cassette containing a sequence of nucleotides with which the nucleic acid binding domain of the fusion protein interacts.

72. (Original) The non-viral delivery system of claim 70, wherein the non-viral delivery system is selected from the group consisting of DNA-ligand complexes, adenovirus-ligand-DNA complexes, direct injection of DNA, $CaPO_4$ precipitation, gene gun techniques, electroporation, liposomes and lipofection.

73. (Previously Presented) The fusion protein of claim 10, wherein the nucleic acid binding domain binds to a targeted nucleic acid molecule with a dissociation constant of less than about 1.0 nanomolar.

74. (Previously Presented) The fusion protein of claim 1 that comprises a DNA binding domain, two ligand binding domains and a transcription modulating domain.

75. (Previously Presented) The fusion protein of claim 1 that forms a dimer when bound to a polynucleotide.

76. (Previously Presented) The fusion protein of claim 1 that is a monomer when bound to a polynucleotide.

77. (Previously Presented) The fusion protein of claim 1 that comprises a second ligand binding domain.

78. (Previously Presented) The fusion protein of claim 77, wherein the second ligand binding domain is the same as the first binding domain.

79. (Previously Presented) The fusion protein of claim 77, wherein the second ligand binding domain is different from the first binding domain.

80. (Previously Presented) The fusion protein of claim 77, wherein the second ligand binding domain is from an intracellular receptor is a nuclear hormone receptor selected from the group consisting of estrogen receptors, progesterone receptors, glucocorticoid-α receptors, glucocorticoid-β receptors, mineralocorticoid receptors, androgen receptors, thyroid hormone receptors, retinoic acid receptors, retinoid X receptors, Vitamin D receptors, COUP-TF receptors, ecdysone receptors, Nurr-1 receptors and orphan receptors.

81. (Previously Presented) The fusion protein of claim 79, wherein the second ligand binding domain is from an intracellular receptor is a nuclear hormone receptor selected from the group consisting of estrogen receptors, progesterone receptors, glucocorticoid-α receptors, glucocorticoid-β receptors, mineralocorticoid receptors, androgen receptors, thyroid hormone
receptors, retinoic acid receptors, retinoid X receptors, Vitamin D receptors, COUP-TF receptors, ecdysone receptors, Nurr-1 receptors and orphan receptors.

82. (Previously Presented) The fusion protein of claim 1 that comprises a heterodimer.

83. (Previously Presented) The fusion protein of claim 82, wherein the heterodimer contains at least three zinc finger modular units, two different ligand binding sites and a transcription modulating domain.

84. (Previously Presented) The fusion protein of claim 1 that comprises a dimer containing first and second monomers, wherein:

the first and second monomers contain a ligand binding domain derived from a nuclear hormone receptor;

at least one monomer has a nucleotide binding domain operatively linked to a ligand-binding domain;

at least one monomer has a transcription regulating domain operatively linked to a ligand-binding domain;

the nucleotide binding domain is a polydactyl C2H2 zinc-finger peptide that binds to a contiguous sequence of nucleotides of about 18 nucleotides.

85. (Previously Presented) The fusion protein of claim 84, wherein the first monomer and the second monomer have a nucleotide binding domain operatively linked to a ligand-binding domain.

86. (Previously Presented) The fusion protein of claim 84, wherein the first monomer and the second monomer have a transcription regulating domain operatively linked to a ligand-binding domain.

87. (Previously Presented) The fusion protein of claim 84, wherein the dimer is a homodimer.

88. (Previously Presented) The fusion protein of claim 84, wherein the dimer is a heterodimer.

89. (Previously Presented) The fusion protein of claim 6, wherein n is 6, whereby the resulting zinc finger has unique specificity for a targeted gene.

90. (New) Isolated cells, comprising the expression vector of claim 26.

91. (New) Isolated cells, comprising the expression vector of claim 27.

92. (New) The isolated cells of claim 90 that comprise eukaryotic cells.

93. (New) The isolated cells of claim 91 that comprise eukaryotic cells.

94. (New) A nucleic acid molecule, comprising a sequence of nucleotides encoding a fusion protein of claim 22.